REMARKS

Applicants again would like to thank the Examiner for providing an office communication concerning this application or proceedings.

Claims 1, 5, 8-11, 19, 25 and 26 are pending in this application.
Claims 1, 11, 19, and 25-26 have been amended.
Claims 2, 3, 4, 6, 7, 12-18, 20-24 and 27-31 are cancelled.

The amendments to claims 1, 11, 19, 25 and 26 will be discussed below.

According to page 2 of the Office Action, claims 1, 2, 5, 8-11, 15, 19, 25, 26 and 31 are allegedly rejected under 35 U.S.C. 103(a) as being unpatentable over Skinhoj et al (US6599529), Saslawski et al (WO99/33448) in view of Gibson et al (US6426340) based on US Provisional Application 60/018202. This rejection is respectfully traversed.

In order to expedite prosecution of this application, Claim 1, 11, 19, 25 and 26 have been further amended to describe the captioned invention which is distinct from the prior arts cited by the learned Examiner. Claims 2 and 31 have now been cancelled. This amendment is being made without prejudice to applicants' rights to file any number of continuation and/or divisional applications for any subject matter disclosed in this application and not presently claimed including compositions. Applicants do not intend to forego any subject matter disclosed in this application and this amendment shall not be considered limiting in terms of prosecution history estoppel.

The dose "200mg" and the phrase 'micronized nimesulide having average particle size below 5 microns' have been included in the claims and support for the same can be found on page No. 7. No prior arts mention the use of 200mg micronized nimesulide having average particle size below 5 microns in fast release layer & extended release layer of the claimed composition as amended herein. Furthermore, the claims have been restricted to the dose of micronized nimesulide i.e. percentage amount of micronized nimesulide, release controlling materials and pharmaceutical acceptable excipients which is in the range from 20 to 70% w/w, 8% to 20% w/w and 30% to 60% w/w respectively of the total composition. The release controlling materials are now clearly mentioned as being present in the extended release layer

of the claimed composition and are biodegradable in nature. Polymers such as cellulose carboxymethyl ether and their salts and polyethylene oxide have been deleted from claim 1 as rate controlling polymers to address the arguments of the learned Examiner during telephonic interview that the claim to a tablet comprising nimesulide in extended release and immediate release layer wherein polymer (control release material) is in the extended release layer, is not commensurate in scope with the results provided for 200 mg nimesulide tablet in Example 10.

The release controlling materials as included in the claims do not include non-biodegradable, inert, polymeric matrix as described in Saslawski et al.

As amended, claim 1 now defines a once-a-day controlled release pharmaceutical tablet composition for peroral administration consisting of a single unit fast release layer and a single unit extended release layer, which comprises 200 mg micronized nimesulide having average particle size below 5 microns as an active drug from 20% to 70% w/w of the tablet composition, one or more release controlling materials in an amount from 8% to 20 % w/w to control the release of said micronized nimesulide from said composition and pharmaceutical excipients from 30% to 60% w/w of the tablet composition, wherein said micronized nimesulide being present in the fast release layer and in the extended release layer and wherein said release controlling materials present in said extended release layer are biodegradable and are selected from the group consisting of methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, cellulose acetate phthalate, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, carbomers, polyalkylene polyols, polycarbophils, gelatins, and gums.

The release controlling materials of the composition do not act as binders or disintegrants.

Claims 11, 19, 25 and 26 as amended herein, includes the same limitation as in claim 1. The same explanation as above for claim 1 is incorporated herein.

The claimed composition that includes these rate controlling materials is not obvious in view of the disclosure of Saslawski et al.

Saslawski et al. teach a multilayer tablet that can be made up of two layers i.e. a first layer (immediate or fast release layer) and second layer (prolonged release layer containing a nonbiodegradable, inert porous polymeric matrix). See page 2, lines 19-30. Saslawski et al teach that the second layer constitutes an inert matrix that does not become eroded and does not swell in an aqueous medium (See page 3, line 33-35) and that the essential constituents of the second prolonged-release layer are polymeric materials which confer on it its inert and nonbiodegradable character. The polymers or copolymers are insoluble in water, not forming a gel and are discharged intact by the body (See page 12, lines 10-15).

It is noted that Saslawski et al neither teach nor suggest the use of biodegradable material in second layer (extended release layer) for prolonging the action of NSAIDs, more preferably nimesulide.

The Examiner argues on page 6 of the Office Action that HPMC used in Saslawski et al as well as in the instant invention is in overlapping concentration ranges, therefore irrespective of what HPMC may be called it should render the same effect or benefit. The Examiner further argues that Saslawski et al teach 0.5 to 25% wt binder such as HPMC (page 11, lines 25-28, page12 lines 3-7) therefore HPMC in Saslawski et al and instant invention would be expected to yield the same effect or benefit since the invention teach overlapping concentration ranges for HPMC.

The applicant argues that in spite of using overlapping concentration of HPMC by applicants of the present invention, the subject matter of invention as claimed herein is clearly distinct from Saslawski et al. The applicants would like to expresses their views along with supportive evidence for the purpose to show that HPMC used by Saslawski would not result in the same benefit or effect as obtained by present invention. The Examiner is requested to consider the disclosure of Muhammad Khan Sarfraz et al, "Naproxen Release from Sustained Release Matrix System and Effect of Cellulose Derivatives" Pak. J. Pharm. Sci., 2006, Vol 19 (3), 244-251, which provides the teaching that low viscosity grades of HPMC are inappropriate for sustaining the release profiles of naproxen and "Handbook of Excipients"; Raymond C Rowe; 5th Edition, Published by Pharmaceutical Press, 2006, Page no. 346-349".

According to Sarfraz, et al., hydrophilic polymer HPMC of low viscosity grades has been used for preparing the sustained release formulation of naproxen. In this study, HPMC has been used either alone or combination with ethyl cellulose (EC) polymer (See table 1). In Formulations F1-F4 wherein HPMC has been used alone (20%-65%) without using another polymer while in formulations F9-F12 wherein HPMC has been used (1%-3%) in combination with EC (5%). The other formulations F5-F8 wherein no HPMC has been used; only ethyl cellulose polymer has been used for preparing the sustained release formulation of naproxen. The in-vitro dissolution studies of all formulations were also performed in this study to predict the achievable plasma drug level. The author of the study discussed that the low viscosity HPMC-based tablets (as used in F1-F4) containing 20%-65% HPMC releases almost 100% of the drug in about 4 hours and rate of drug release could not be sustained for more than 4 hours. Hence, low viscosity grades of HPMC are inappropriate for sustaining the release profiles of naproxen (See fig1). But when HPMC-EC mixture was used wherein the amount of HPMC is 1%, 1.5%, 2%, 3% and amount of EC is 5%, showed a decreased release rate of naproxen. The release rate of naproxen in eight hours was 38%, 86%, 98 100% from the formulation containing 1%, 1.5%, 2%, 3% HPMC respectively. By submitting the evidence of comparison of two dissolution profile of two kinds of formulations- (i) Percentage release rate of F1-F4 wherein HPMC has been used alone (20%-65%) without using another polymer (ii) Percentage release rate of F9-F12 wherein HPMC has been used (1%-3%) in combination with EC (5%); we infer that alone low viscosity grade HPMC is not appropriate for sustaining the release of drug. As evidently known by Handbook of Excipients that HPMC is available in different grades and viscosities which can be used as a tablet binder, film-coating and as a matrix for use in extended-release tablet formulation depending upon viscosity, concentration and molecular weight grades. Concentration between 2% and 5% w/w may be used as a binder in wet- and dry-granulation. High viscosity grades may be used to retard the release of drugs from a matrix at level of 10-80% w/w in tablet or capsules while low-viscosity grades are used for film forming and binder.

Moreover, Saslawski et al has not disclosed different grades or viscosity of HPMC and its use other than binder or disintegrator. Saslawski et al provide release of 9 hours (Once-daily dosing) due to the presence of non-biodegradable polymer, not by the presence of binder e.g. HPMC. In all examples of Saslawski, HPMC has been used in an amount which acts as a binder, not for sustaining the release of drug for 9 hours to provide once-daily dosing. Hence

person skilled in the art would never use HPMC taught by Saslawski for sustaining the release of drug. Therefore, HPMC-based formulation prepared according to Saslawski (even used upto 25%) will not provide the same benefit or effect until formulation contains additional non-biodegradable polymer. Saslawski et al teaches away from using hydrophilic/biodegradable polymer for sustaining the release of drug. While the composition prepared according to the present invention does not contain any non-biodegradable polymer but also it contains hydrophilic polymers which are biodegradable in nature and/or swellable in water thus, provides once-daily administration of nimesulide.

The inventors insist that person skilled in the art would never confuse between HPMC as a binder and HPMC as a release controlling material which is well understood to be used based upon its viscosity and molecular weight grades. As known by a skilled person, when HPMC is referred to be used as a binder it is used in the particular grade and viscosity which will only function as a binder and not function as a release controlling agent even used in any amount as shown in Sarfraz.

Applicant further argues that the Examiner should not speculate his own understanding over the prior art teaching which is not intended and mentioned in the prior arts. In doing this, the Examiner is engaging in impermissible hindsight.

> To reach a proper determination under **35 U.S.C. 103**, the examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of applicant's disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences," conduct the search and evaluate the "subject matter as a whole" of the invention. The tendency to resort to "hindsight" based upon applicant"s disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art. (MPEP 2142).

HPMC as a release controlling material has not been used by Saslawski et al in the invention WO'448. If the HPMC in Saslawski's invention would also act as a release controlling material and would produce same benefit as produced by the instant invention; then Saslawski et al should have mentioned it clearly in one of the alternative embodiment of the invention. Alternatively, Saslawski should have included HPMC under rate controlling material as in the case of US4167558 (Col 3, lines 43-60) and US4571333 (Col 6, lines 19-

50) wherein HPMC has been used as release controlling materials. Moreover, Saslawski's invention describes to make composition of NSIAD by utilizing non-biodegradable polymer as rate controlling material whilst applicant's intention to make composition which is free of any non-biodegradable polymer

Saslawski et al has not disclosed different grades or viscosity of HPMC and its use other than binder or disintegrator. Saslawski et al provide release of 9 hours (Once-daily dosing) due to the presence of non-biodegradable polymer, not by the presence of binder e.g. HPMC. In all examples of Saslawski, HPMC has been used in an amount which acts as a binder, not for sustaining the release of drug for 9 hours to provide once-daily dosing. Hence person skilled in the art would never use HPMC taught by Saslawski for sustaining the release of drug. Therefore, HPMC-based formulation prepared according to Saslawski (even used upto 25%) will not provide the same benefit or effect until formulation contains additional non-biodegradable polymer. Saslawski et al teaches away from using hydrophilic/biodegradable polymer for sustaining the release of drug. While the composition prepared according to the present invention does not contain any non-biodegradable polymer but also it contains hydrophilic polymers which are biodegradable in nature and/or swellable in water thus, provides once-daily administration of nimesulide.

The claim as amended herein recites 200mg micronized nimesulide having average particle size below 5 microns as an active drug from 20% to 70% w/w of the tablet composition, amount of said release controlling material in the range between 8% w/w to 20% w/w of the total composition to control the release of nimesulide over a period of time and amount of pharmaceutical acceptable excipients in the range from 30% to 60% w/w of the total composition.

"All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When evaluating claims for obviousness under **35 U.S.C. 103**, all the limitations of the claims must be considered and given weight, including limitations which do not find support in the specification as originally filed (i.e., new matter). *Ex parte Grasselli*, 231 USPQ 393 (Bd.

App. 1983) *aff'd mem.* 738 F.2d 453 (Fed. Cir. 1984) (Claim to a catalyst expressly excluded the presence of sulfur, halogen, uranium, and a combination of vanadium and phosphorous. Although the negative limitations excluding these elements did not appear in the specification as filed, it was error to disregard these limitations when determining whether the claimed invention would have been obvious in view of the prior art.) (See MPEP 2143.03)

Saslawski et al. teach away from Claim 1, as amended herein. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant" *In re Gurley* 27 F.3d 551, 553 (Fed. Cir. 1994); *see KSR*, 127 S. Ct. at 1739-40 (explaining that when the prior art teaches away from a combination, that combination is more likely to be nonobvious).

One of ordinary skill in the art following the teachings of Saslawski et al. would be taught to formulate a composition having first outer layer allowing immediate release of a first active substance (page 2, line 3-26) and a second layer containing a nonbiodegradable, inert porous polymeric matrix (page 2, lines 27-30) and that these polymers or copolymers [are] insoluble in water (but not forming a gel either upon immersion in an aqueous medium) (page 22, lines 8-15). One of ordinary skill in the art would find no motivation to provide a formulation as defined in independent claims 1, 11, 25, 26 and dependent claim 19 of nimesulide with single unit fast release layer comprising micronized nimesulide having average particle size below 5 microns and single unit extended release layer comprising micronized nimesulide having average particle size below 5 microns and biodegradable release controlling materials selected from a group consisting of methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, cellulose acetate phthalate, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, carbomers, polyalkylene polyols, polycarbophils, gelatins, and gums in an amount effective to control the release of nimesulide from the extended release layer.

We have already submitted a number of references with last response dated Aril 24, 2009 that describe that these release controlling materials are biodegradable and/or gel or swell and erode in the presence of water. As described above, these release controlling materials differ from those disclosed in Saslawski et al.

The Examiner states on page 4 of the Office Action that Saslawski et al. allows for the inclusion of NSAID compounds which would suggest the inclusion of Nimesulide (or the sulfonanilide compound class). The Examiner argues on page 5 of the Office Action "*Skinhoj et al. teach use of naproxen and nimesulide and suggest that both naproxen and nimesulide are equivalent. For this reason, it would have been obvious to artisan in the field to modify the invention of Saslawski et al. by substituting the naproxen taught therein with the nimesulide taught by Skinhoj et al.*"

It is emphasized that neither nimesulide nor any other sulfonanilide derivative has been disclosed by Saslawski et al. Although Skinhoj et al. describes certain types of NSAIDs, that include nimesulide and naproxen but it does not teach or suggest micronized nimesulide having average particle size below 5 microns. Applicant herein argues that no prior arts (either Skinhoj et al. or Saslawski et al.) mention the use of micronized nimesulide having average particle size below 5 microns. (*See Merck & Co., Inc., V. Biocraft Laboratories*, United States Court of Appeals, Federal Circuit – 874 F.2d 804).

Therefore, the Examiner has not established a *prima facie* case of obviousness.

The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also *KSR*, 550 U.S. 82 USPQ2d at 1396.

Claim 1, as amended herein, now specifically recites- (i) 200 mg micronized nimesulide having average particle size below 5 microns and; (ii) release controlling materials of the extended release layer which are biodegradable in nature and which hydrate and swell in presence of water or body fluids, thus the release controlling materials are NOT nonbiodegradable, inert porous polymeric matrix like the copolymers of (meth)acrylic acid derivatives as required by Saslawski et al

This clearly distinguishes the present invention from the teachings of Saslawski et al. which neither teaches nor suggests a once-a-day controlled release tablet composition of a single unit fast release layer comprising micronized nimesulide having average particle below 5 microns and a single unit extended release layer comprising micronized nimesulide having average particle below 5 microns and one or more biodegradable release controlling materials selected from a group consisting of methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, cellulose acetate phthalate, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, carbomers, polyalkylene polyols, polycarbophils, gelatins, and gums.

Therefore, it is clear that the claimed invention is not obvious Saslawski et al.

In KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727, 167 L. ED.. 2nd 705 (2007), the Supreme Court held that the obviousness analysis of *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 86 S.Ct. 684, 15L. Ed. 2nd 545 (1966), controls an obviousness inquiry. The Graham obviousness factors include "the scope and content of the prior art" and the "differences between the prior art and the claims". KSR, 127 S.Ct. at 1734 (quoting Graham, 383 U.S. at 17-18). Prima facie obviousness may be overcome by a showing of commercial success.

Although, as stated above, it is applicants' position that no prima facie showing of obviousness has been made, as further evidence that the claimed invention is not obvious over Saslawski et al., is the declaration of Dr. Rajesh Jain, one of the inventors of the claimed subject matter, submitted on dated April 24, 2009.

The decision on patentability must be made based upon consideration of all the evidence, including the evidence submitted by the examiner and the evidence submitted by the applicant. A decision to make or maintain a rejection in the face of all the evidence must show that it was based on the totality of the evidence. Facts established by rebuttal evidence must be evaluated along with the facts on which the conclusion of obviousness was reached, not against the conclusion itself. *In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 (Fed.

Cir. 1990). Therefore, the Examiner must consider the evidence in Dr. Jain's declaration and the evidence of commercial success.

Affidavits or declarations, when timely presented, containing evidence of criticality or unexpected results, commercial success, long-felt but unsolved needs, failure of others, skepticism of experts, etc., must be considered by the examiner in determining the issue of obviousness of claims for patentability under **35 U.S.C. 103**. The Court of Appeals for the Federal Circuit stated in *Stratoflex, Inc. v. Aeroquip Corp.* 713 F.2d 1530, 1538, 218 USPQ 871, 879 (Fed. Cir. 1983) that "evidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness." Such evidence might give light to circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or unobviousness, such evidence may have relevancy. *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966); *In re Palmer*, 451 F.2d 1100, 172 USPQ 126 (CCPA 1971); *In re Fielder,* 471 F.2d 640, 176 USPQ 300 (CCPA 1973).

The weight attached to evidence of secondary considerations by the examiner will depend upon its relevance to the issue of obviousness and the amount and nature of the evidence. Note the great reliance apparently placed on this type of evidence by the Supreme Court in upholding the patent in *United States v. Adams*, 383 U.S. 39,148 USPQ 479 (1966).

To be given substantial weight in the determination of obviousness or nonobviousness, evidence of secondary considerations must be relevant to the subject matter as claimed, and therefore the examiner must determine whether there is a nexus between the merits of the claimed invention and the evidence of secondary considerations. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 305 n.42, 227 USPQ 657, 673-674 n. 42 (Fed. Cir. 1985), *cert. denied*, 475 U.S. 1017 (1986). The term "nexus" designates a factually and legally sufficient connection between the objective evidence of nonobviousness and the claimed invention so that the evidence is of probative value in the determination of nonobviousness. *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 7 USPQ2d 1222 (Fed. Cir.), *cert. denied*, 488 U.S. 956 (1988).

If, after evaluating the evidence, the examiner is still not convinced that the claimed invention is patentable, the next Office action should include a statement to that effect and identify the

reason(s) (e.g., evidence of commercial success not convincing, the commercial success not related to the technology, etc.). See *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 7 USPQ2d 1222 (Fed. Cir.), *cert. denied*, 488 U.S. 956 (1988).

Evidence traversing rejections, when timely presented, must be considered by the examiner whenever present. Where the evidence is insufficient to overcome the rejection, the examiner must specifically explain why the evidence is insufficient. General statements such as "the declaration lacks technical validity" or "the evidence is not commensurate with the scope of the claims" without an explanation supporting such findings are insufficient (MPEP 716.01 Section B).

In the interview summary dated July 21, 2009, the Examiner pointed out that the claims to a tablet comprising nimesulide in extended release and immediate release layer wherein polymer (control release material) is in the extended release layer is not commensurate in scope with the results provided for 200 mg nimesulide tablet in Example 10. Applicant explains that the claims as amended herein exclude cellulose carboxymethyl ether & their salt (which includes croscarmellose sodium) and polyethylene oxide (which includes polsorbate 80) as a release controlling material from the list of polymer originally filed. The said two release controlling materials present in fast release layer of Example 10, cannot be present in extended release layer of Example 10 as a release controlling material. Furthermore amended claims now recite that the release controlling material is present in extended release layer. The Applicant reiterates that the claims as amended herein are commensurate in scope with Example 10.

When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the applicant to show unexpected results over the entire range of properties possessed by a chemical compound or composition. See, e.g., *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. *Id.* For example, a showing of unexpected results for a single member of a claimed subgenus, or a narrow portion of a claimed range would be sufficient to rebut a *prima facie* case of obviousness if a skilled artisan "could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof." *In re Clemens*, 622 F.2d 1029,

1036, 206 USPQ 289, 296 (CCPA 1980) (Evidence of the unobviousness of a broad range can be proven by a narrower range when one skilled in the art could ascertain a trend that would allow him to reasonably extend the probative value thereof.).

In regard to Gibson, this reference has no relevance whatsoever to the present claims. It does not bridge the gap with any mention of nimesulide or bilayered once-a-day controlled release tablet as claimed herein; it only mentions use of silicon dioxide in immediate and controlled release formulation, which the Examiner would agree is already well-established in the art. There is no suggestion or motivation in the combination of the cited references to combine the references to develop a once-a-day controlled release composition of nimesulide as claimed in this application and no reasonable expectation of success to achieve its success in the market place.

Neither Skinhoj nor Saslawski et al nor Gibson et al., singly or in combination, teach or suggest a once-a-day controlled release composition of nimesulide consisting of single unit fast release layer comprising micronized nimesulide having average particle below 5 microns and single unit extended release layer comprising micronized nimesulide having average particle below 5 microns and one or more biodegradable release controlling materials, wherein the release controlling materials present in the extended release layer are specified from a group consisting of methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, cellulose acetate phthalate, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, carbomers, polyalkylene polyols, polycarbophils, gelatins, and gums.

In light of the scope and content of the prior art and in light of the differences between the prior art and the claims, applicant respectfully submits that claim 1, as amended herein, is patentable over the combined teachings of Skinhoj et al, Saslawski et al and Gibson et al. Claims 5, 8, 9, and 10 (previously amended) and claim 19 (currently amended) depend directly or indirectly, on claim 1, as amended herein. Under 35 U.S.C. 112, fourth paragraph, "a claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers". "If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious". MPEP 2143.03; *In refine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants respectfully submit that all of the claims as herein, are patentable over the combined teachings of Saslawski et al and Gibson et al.

Therefore, it is respectfully requested that the rejection be withdrawn.

It is submitted that the present application is in condition for allowance and favorable consideration is respectfully requested. If any issues remain, please contact the undersigned

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